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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,633	SANLI ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1 136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1 704(b)

Status

1)☒ Responsive to communication(s) filed on *06 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31,40-43 and 49-52* is/are pending in the application.

4a) Of the above claim(s) *19-31 and 49-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-18 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17 2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Applicants preliminary amendment of canceling claims 38, 39, 44-48 and 53-58, Paper No. 7, 3/6/2003, is acknowledged. Claims 1-37, 40-43 and 49-52 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-18 and 40-43 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that examination of group I, drawn to an isolated nucleic acid encoding 2, 5-diketo-D-gluconic acid reductase A and group II, drawn to an isolated nucleic acid encoding 2, 5-diketo-D-gluconic acid reductase B, will each require a common search strategy in the same class/subclass and thus no serious additional search burden is encompassed by the additional examination of group II in addition to group I. Applicants argument is not found persuasive because while the searches for the each of the groups overlap, they are not coextensive, as each of the different groups are drawn to variants of different nucleic acid molecules which since they are different molecules, require different independent searches and are thus patentably distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 19-37 and 49-52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7.

Priority

Applicants claims of priority to U.S. Provisional application 60/259,527, filed January 3, 2001 which is incorporated in its entirety by reference is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures, Paper No. 5, filed 3/12/2002, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

Applicants abstract recites in a number of places "nucleic acid comprises" (line 5 and line 7) and "polypeptide, comprises" (line 9). This should be amended to "nucleic acid comprising" and "polypeptide, comprising".

Claim Objections

Claims 1-18 are objected to because of the following informalities:

Claims 1-18 each recite "nucleic acid". It is suggested that applicants amend this to "nucleic acid sequence" or "nucleic acid molecule".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 6, 7, 8, 10-18 and 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 11 are indefinite in that it is confusing in the recitation "... further comprising a plurality of codons...." Specifically the claim is confusing because the claim is drawn to the nucleic acid of claim 1, which is drawn to a degenerate variant of SEQ ID NO: 1, but the claim recites that the nucleic acid "further comprising a plurality of codons". It is unclear if it is applicants intent that the referred to plurality of codons is "in addition" to but not included within the degenerate variant nucleotide sequence of claim 1 or is the referred to plurality of codons a further limitation. If applicants intent is the later, that the plurality of codons is a further limitation of the nucleic acid of claim 1, it is suggested that applicants delete "further" from claim 3, as recitation of the word "further" is not necessary in the claim which further limits a claim from which it depends.

Claim 6, 14 and 40-43 are indefinite in that the recitation "...an expression vector operably linked to an expression control sequence" is unclear. Is it not applicants intent

that the expression vector claimed comprises the nucleic acid of claim 1 operably linked to an expression control sequence in contrast to the expression vector itself being operably linked to an expression control sequence. Presumably the expression vector comprises an expression control sequence, as opposed to being operably linked to an expression control sequence.

Claims 7-9 and 15-17 are indefinite in that they are each drawn to the nucleic acid of claims 1 or 10, respectively, wherein said nucleic acid is placed within a specific situation/environment that does not further limit or change the nucleic acid of claims 1 or 10, respectively. Thus the claims do not further limit claims 1 and 10, respectively, from which they depend. For instance, in claim 7, the fact that the nucleic acid of claim 1 is within in an isolated cell does not change the nucleic acid of claim 1. Further, applicants claims do not require that the nucleic acid of claim 1 be comprised within the referred to expression vector nor operably linked to an expression control sequence. An amendment of claims 7 (or claim 15)such as "An isolated cell comprising an expression vector comprising the nucleic acid of claim 1 (or claim 10), operably linked to an expression control sequence" may help applicants overcome this rejection. A similar amendment of claims 8 and 16 would help applicants overcome this rejection. Claims 9 and 17 are similarly indefinite in that the recitation "...and wherein an isolated cell or a progeny of said cell is transfected with said vector" does not further limit the claimed nucleic acid.

Claim 10 (11-18 dependent on) is indefinite in that it is confusing in that it is appears to be a duplicate of claim 1. Claim 10 is drawn to an isolated nucleic acid

comprising a sequence having a GC content of from about 55% to 67% and encoding a polypeptide having the amino acid sequence of SEQ ID NO: 5. Claim 1 is drawn to drawn to an isolated nucleic acid comprising a degenerate variant of the nucleotide sequence of SEQ ID NO: 1 having a GC content of from about 55% to 67%. As SEQ ID NO: 1 encodes SEQ ID NO: 5, any degenerate variant of SEQ ID NO: 1 must also encode SEQ ID NO: 5, and thus claim 1 is drawn to an isolated nucleic acid comprising a sequence having a GC content of from about 55% to 67% and encoding a polypeptide having the amino acid sequence of SEQ ID NO: 5. Thus claims 1 and 10 are duplicates as are each of the claims that depend from claims 1 and 10 duplicates of each other.

For similar reasons as discussed above with respect to claims 1 and 10, claims 40 and 41 and 42 and 43 are also duplicates.

Claim 18 is indefinite in that the recitation "wherein the GC content is effective for producing an average codon bias in enteric bacteria of from greater than about 44% to about 66%" is unclear. It appears that applicants reference to "from greater than about 44% to about 66%" refers to the "average codon bias in enteric bacteria". How is codon bias related to a percentage??

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 and 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (Science, Vol 230, pages 144-149, 1985) and Mohsen et al. (Gene, Vol 160, pages 263-267, 1995).

Anderson et al. teach the isolation and cloning of the cDNA which encodes 2, 5-diketo-D-gluconic acid reductase A having the sequence of instantly disclosed SEQ ID NO: 1. It is noted that the GC content of the instantly disclosed SEQ ID NO: 1 is 68%.

Mohsen et al. teach the high-level expression of an altered cDNA encoding human isovaleryl-CoA dehydrogenase (IVD) in *Escherchia coli*. Specifically Mohsen et al. teach that the cloned human IVD cDNA coding region includes a region with a high G + C content (73.5%). Mohsen et al. teach that bias codon usage in different organisms has been recognized as a possible mechanism for regulation of protein expression, and thus altered the codon usage of the region with high G + C content to mimic codon usage of highly expressed proteins in *E. coli* (See Figure 1A) as a means of increasing the expression of the cloned human IVD cDNA in *E. coli*. Mohsen et al. altered the IVD cDNA such that the G + C content in the corresponding are changed from 59.3% in the wildtype to 53.7% in the modified cDNA. The altered codons taught by Mohsen et al. included valine, alanine arginine and glycine.

One of ordinary skill in the art at the time of filing would have been motivated to express the cDNA taught by Anderson et al. in *E. coli* so that it could be easily manipulated and expressed. One of ordinary skill in the art would have been further motivated to alter the codon usage of the cDNA taught by Anderson et al., SEQ ID NO: 1 such that the codons usage reflected those used routinely in *E. coli* so as to increase

the production of the encoded 2, 5-diketo-D-gluconic acid reductase A protein. Such alterations in codon preference as taught by Mohsen et al. would result in a decrease in the G + C content to less then it is in the wildtype, which is 68%, thus the G + C content would be in the range of 55% to 67%. The many advantages of recombinant production of useful proteins in *E. coli* are well known within the art. These advantages include the ability to produce much larger quantities of the protein, being able to produce the protein in more easily handled organism, reducing the number of steps necessary for the purification of a protein and producing the protein in a purer form by using an organism that does not include naturally occurring contaminants of the protein. The reasonable expectation of success comes from the high level of skill in the art in the area of recombinant expression of proteins.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
April 4, 2003